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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/052,926	01/16/2002	Jeffrey R. Sampson	2003309-0027 (Agilent 10	1042

7590 06/12/2008  
AGILENT TECHNOLOGIES, INC.  
Legal Department, DL429  
Intellectual Property Administration  
P.O. Box 7599  
Loveland, CO 80537-0599

EXAMINER
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MUMMERT, STEPHANIE KANE

ART UNIT	PAPER NUMBER
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1637

MAIL DATE	DELIVERY MODE
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06/12/2008

PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Advisory Action</b> <b>Before the Filing of an Appeal Brief</b>	<b>Application No.</b> 10/052,926	<b>Applicant(s)</b> SAMPSON, JEFFREY R.	
	<b>Examiner</b> STEPHANIE K. MUMMERT	<b>Art Unit</b> 1637	

**--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --**

THE REPLY FILED 09 May 2008 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE.

1. ☒ The reply was filed after a final rejection, but prior to or on the same day as filing a Notice of Appeal. To avoid abandonment of this application, applicant must timely file one of the following replies: (1) an amendment, affidavit, or other evidence, which places the application in condition for allowance; (2) a Notice of Appeal (with appeal fee) in compliance with 37 CFR 41.31; or (3) a Request for Continued Examination (RCE) in compliance with 37 CFR 1.114. The reply must be filed within one of the following time periods:

- a) ☐ The period for reply expires \_\_\_\_\_ months from the mailing date of the final rejection.  
 b) ☒ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.

Examiner Note: If box 1 is checked, check either box (a) or (b). ONLY CHECK BOX (b) WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### NOTICE OF APPEAL

2. ☐ The Notice of Appeal was filed on \_\_\_\_\_. A brief in compliance with 37 CFR 41.37 must be filed within two months of the date of filing the Notice of Appeal (37 CFR 41.37(a)), or any extension thereof (37 CFR 41.37(e)), to avoid dismissal of the appeal. Since a Notice of Appeal has been filed, any reply must be filed within the time period set forth in 37 CFR 41.37(a).

#### AMENDMENTS

3. ☐ The proposed amendment(s) filed after a final rejection, but prior to the date of filing a brief, will not be entered because  
 (a) ☐ They raise new issues that would require further consideration and/or search (see NOTE below);  
 (b) ☐ They raise the issue of new matter (see NOTE below);  
 (c) ☐ They are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or  
 (d) ☐ They present additional claims without canceling a corresponding number of finally rejected claims.

NOTE: \_\_\_\_\_. (See 37 CFR 1.116 and 41.33(a)).

4. ☐ The amendments are not in compliance with 37 CFR 1.121. See attached Notice of Non-Compliant Amendment (PTOL-324).  
 5. ☐ Applicant's reply has overcome the following rejection(s): \_\_\_\_\_.  
 6. ☐ Newly proposed or amended claim(s) \_\_\_\_\_ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).  
 7. ☒ For purposes of appeal, the proposed amendment(s): a) ☐ will not be entered, or b) ☒ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.  
 The status of the claim(s) is (or will be) as follows:  
 Claim(s) allowed: \_\_\_\_\_.  
 Claim(s) objected to: \_\_\_\_\_.  
 Claim(s) rejected: 1-35,67-101 and 144-149.  
 Claim(s) withdrawn from consideration: \_\_\_\_\_.

#### AFFIDAVIT OR OTHER EVIDENCE

8. ☐ The affidavit or other evidence filed after a final action, but before or on the date of filing a Notice of Appeal will not be entered because applicant failed to provide a showing of good and sufficient reasons why the affidavit or other evidence is necessary and was not earlier presented. See 37 CFR 1.116(e).  
 9. ☐ The affidavit or other evidence filed after the date of filing a Notice of Appeal, but prior to the date of filing a brief, will not be entered because the affidavit or other evidence failed to overcome all rejections under appeal and/or appellant fails to provide a showing a good and sufficient reasons why it is necessary and was not earlier presented. See 37 CFR 41.33(d)(1).  
 10. ☐ The affidavit or other evidence is entered. An explanation of the status of the claims after entry is below or attached.

#### REQUEST FOR RECONSIDERATION/OTHER

11. ☒ The request for reconsideration has been considered but does NOT place the application in condition for allowance because:  
See Continuation Sheet.  
 12. ☐ Note the attached Information *Disclosure Statement*(s). (PTO/SB/08) Paper No(s). \_\_\_\_\_.  
 13. ☐ Other: \_\_\_\_\_.

/GARY BENZION/  
 Supervisory Patent Examiner, Art Unit 1637

/Stephanie K. Mummert/  
 Patent Examiner, Art Unit 1637

Continuation of 11. does NOT place the application in condition for allowance because: Applicant's arguments have been considered, but they are not persuasive. First, it is noted that Applicant is arguing a scope of the invention that is not commensurate with the claims as currently stated. Applicant is arguing the inclusion of two different complementary base pair analogs within unstructured nucleic acids. That argument only addresses claims 5 and 71. The independent claim which includes the two different complementary base pair analogs does not explicitly require that the nucleic acid has to be in the form of UNA (unstructured nucleic acids) as argued by Applicant.

Regarding Kutayavin, Applicant argues that "Kutayavin is merely directed to inter-molecular interactions and discloses oligonucleotides in which 'complementary positions in both SBC ODNs are modified into a matched pair of SBC ODNs of the present invention so that the pair of the matched set does not form a stable hybrid'" (p. 12 of remarks). While Applicant's arguments are noted, that Kutayavin does not explicitly teach that these nucleotides would also result in a reduction in intramolecular secondary structure, it is noted in response that these modified nucleotides would inherently reduce secondary structure in an intra-molecular setting, in addition to the findings regarding inter-molecular interactions. If the hybrids formed between these nucleotides are reduced inter-molecularly, hybrids formed intra-molecularly would also be reduced, resulting in reduced secondary structure. It is also noted that Kutayavin teaches the same modified analogs as claimed in dependent claim 33-34 and so would be expected to function in the same manner as claimed.

Furthermore, Applicant is arguing against Kutayavin alone, when Kutayavin is relied upon primarily for the teaching of the inclusion of 2-aminoadenosine and 2-thiothymidine nucleotides to reduce secondary structure and this teaching is provided in view of the teachings of Church and Morgan. Morgan also teaches the inclusion of modified or analog nucleotides which reduce secondary structure in the nucleic acid molecule. Morgan specifically teaches the inclusion of inosine to reduce secondary structure. Kutayavin does not stand alone and renders the claims obvious only in view of the combined teachings of Church and Morgan, to achieve nucleic acids in which secondary structure is reduced through the inclusion of analog nucleotides.

Regarding Applicant's arguments "the use of UNA nucleotides to decrease intra-molecular interactions might in hindsight appear to be a straightforward extension of prior art methods" (p. 11 of remarks) are also noted. However, it is noted again that the base rejection of the independent claim does not require unstructure nucleic acids where the secondary structure is reduced. The claim only requires that the secondary structure of the nucleic acid is reduced through the inclusion of modified or analog nucleotides. The rejections are maintained because the prior art teaches the inclusion of modified nucleotides for the reduction in secondary structure as taught by Morgan and Kutayavin. The prior art also teaches the method of nanopore sequencing as taught by Church. These references in combination render the claimed invention obvious.

It is also noted, in response to Applicant's arguments regarding KSR, that KSR also advises that the combination of known prior art elements to achieve a predictable result is another rationale to support a finding of obviousness. While Applicant's arguments regarding a lack of motivation are noted, it is noted in response that one of ordinary skill would have known to look to the known prior art elements of analog nucleotides like inosine, 2-thiothymidine, 2-aminoadenosine, which are also known to reduce binding and to reduce secondary structure. Therefore, even in the absence of an explicit motivation, one of ordinary skill would have recognized that including modified nucleotides in a nucleic acid molecule would achieve a predictable result of reduction in secondary structure. Therefore, the rejection is maintained.

Applicant traverses the rejection of dependent claims in view of Lizardi and in view of Thorp. The arguments against these dependent claims are based on the arguments addressed above. These rejections are maintained for the reasons previously stated above.